

## REMARKS

Claims 1-3, 6-21 and 24-72 are pending in this application and pending claims 1-3, 6-21 and 24-72 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 68-69 stand rejected under 35 U.S.C. § 102(b) as anticipated by Christen, et al. These rejections are addressed by the above amendments and the following arguments.

### The Amendments

The specification is amended on page 23, line 29, to correct an obvious typographical error. The first compound listed on line 29 is "3-Iodophenoxyacetic acid," and as explained in the attached Declaration of Dr. Venkataraman Bringi, this is clearly erroneous. The correct compound, which would be recognized by the skilled person in view of the characterization of the listed compounds as "auxin-related growth factors," is "4-Iodophenoxyacetic acid," and the specification is amended herein to correct this obvious error. The specification is also amended to replace Tabel 2 with a clean copy of the same Table. No changes in the Table are introduced, and the copy is the same as Table 2 of Application No. PCT/US97/08907 incorporated in the present application by reference.

Claim 1 is amended to correct an inadvertant and obvious typographical error; the singular article "an" appears before a plural noun (esters). Also in claim 1, the word "or" was omitted between "compounds" and "esters thereof" (see dependent claim 3). Both these obvious errors are corrected herein. Claims 24-26 and 71 are amended for consistency with claims 2 and 18 from which they depend. Claim 27 is amended to provide an alternative statement of the relationship between silver and jasmonic acid that is recited in the claim. Claims 29 and 34 are amended to replace the tradename "SKF-525A" with the definition of this material from the specification, pages 25, lines 27-28. Claim 32 is amended to replace "auxin-related growth regulator" with the list of suitable regulator compounds provided in the specification on pages 23-25. Claim 43 and 45-48 are amended to insert missing articles; this obvious grammatical revision does not introduce new matter. Claim 50 is amended to substitute a definition from the specification into the claims in place of the term defined. This amendment has no effect on the scope of the claim; the amendment is not necessary for patentability and is made only for the convenience of the Examiner as requested in the Office Action. Claims 68 and 69 are amended

to eliminate one of two elements in a Markush group. Claim 72 is drawn to methods utilizing enhancing precursor material as disclosed in the specification on page 25, lines 26-27, and the claim is amended to recite the constraints on the amount of enhancing precursor material as those constraints are discussed in the specification on page 21, lines 9-28.

The above amendments do not change the scope of claims other than claims 68-69 and 72. Applicants submit that these amendments are fully supported in the application as filed and add no new matter to the application. Entry of these amendments is respectfully requested.

#### **Rejection under 35 U.S.C. § 112, Second Paragraph**

Claims 1-3, 6-21 and 24-72 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

Claim 1 stands rejected as confusing because of a grammatical inconsistency resulting from the typographical errors in the claim; these errors are acknowledged and corrected in the present Amendment. In view of this amendment, there is no inconsistency between claim 1 and claim 30. Claims 24-26, 43, 45-48 and 71 stand rejected because of obvious typographical errors which are corrected in this Amendment. Applicants appreciate the acknowledgement by the Examiner that “a saccharide” as used in both the amended claims and those of Yukimune, et al., are equally clear.

Claim 15 recites the well known enzymes of the ethylene synthesis pathway as described in the specification on page 22 and in standard text books, including “Plant Physiology,” by Salisbury, F.B., and C.W. Ross, Wadsworth, Belmont, California, 1992, esp. pp. 357-407 and 531-548, and “Plant Hormones: Physiology, Biochemistry and Molecular Biology,” Peter J. Davies, ed., Kluwer Academic Publishers, 1995. See especially Chapter B4 by McKeon, et al., in Davies, 1995 entitled “Biosynthesis and Metabolism of Ethylene,” pp. 118-139, a copy of which is attached hereto, which shows standard abbreviations on page 118, including the abbreviation on “ACC” for 1-aminocyclopropane-1-carboxylic acid.

Claim 27, as amended, recites the preferred relationship between two enhancement agents when the enhancement agents silver ion and jasmonate-related compound are used together. These enhancement agents are described in the specification (see specification, page 7, lines 24-26, and page 29, lines 19-25), and the antecedent basis for their recitation is in claim 1: "nutrient media comprises one or more enhancement agents." Claims 29 and 34 are amended to spell out terms abbreviated in the original claims.

Claim 72 is amended herein to clarify the scope of the claim in view of this disclosure. The amount of enhancing precursor material described on page 25, lines 26-27, used to provide useful enhancement to taxane production will depend on the culture conditions as taught in the specification on page 21, lines 9-28, and the particular amount of  $\beta$ -phenylalanine for particular culture conditions may be determined by the skilled worker in view of the guidance in the specification.

With respect to the phrase "auxin-related growth regulators" in claim 32, Applicants submit that no definition is needed for this well-known class of compounds. Literature discussions of this class of compounds are of record in the present application (see, e.g., George, ed., "Plant Propagation by Tissue Culture," Exegetics Ltd. (1993), pp. 421-425, and references cited in Davies, et al., *Plant Hormones: Physiology, Biochemistry and Molecular Biology*) and examples are provided in the specification for guidance. Thus, the ordinary worker would have no difficulty recognizing this well known group of compounds in the claims. However, to facilitate prosecution, the phrase "auxin-related growth factors" is replaced in claim 32 by the list of such growth factors provided in the specification on pages 23-25.

Claim 43 further limits claim 42 by indicating particular components that differ between the compositions of the first and second media. Specifically, nitrate and saccharide levels differ, in that the nitrate level is lower and the saccharide level is higher in the second medium than in the first. Comparison of the compositions of the two media to identify which medium has the higher level of each of these components is easily within the skill of the ordinary worker in this art, and Applicants do not believe that the ordinary worker will have any difficulty in determining whether the media used in a particular process are infringing or not. Applicants respectfully request that the Examiner point out with particularity what about the very specific recitation of two distinct compositions ("a first composition" and "a second composition which

induces taxane production") and the relationship between them ("the concentration of [nitrate or a saccharide] is [lower or higher, respectively] in the second medium than in the first medium") would confuse the skilled worker.

Claim 49 recites that "the medium which induces taxane production is replenished", and thus the medium replenished according to claim 49 is clear from its antecedent basis in claim 42. Claim 50 is amended in parallel with claim 49. Applicants submit that the present claims, as amended, are clear and should not be rejected under 35 U.S.C. § 112.

**Rejection under 35 U.S.C. § 102(b)**

Claims 68-69 stand rejected under 35 U.S.C. § 102(b) as anticipated by Christen, et al. This rejection is respectfully traversed.

Claims 68-69 are amended to remove recitation of amino acids generally, without prejudice to Applicant's claims to use of specific amino acids, such as glutamine (claim 65) or phenylalanine (claim 72). Christen, et al., do not disclose the use of polyamines recited in amended claims 68-69, and therefore, rejection of these claims under 35 U.S.C. § 102 should be withdrawn.

Applicants believe that the subject application is now in condition for allowance, and such disposition is earnestly solicited. If the Examiner believes that prosecution might be furthered by discussing the application with Applicants' representative, in person or by telephone, we would welcome the opportunity to do so.

Respectfully submitted,

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**APPENDIX A**  
**VERSION OF PARAGRAPHS WITH MARKINGS**  
**U.S. Application No. 08/479,809**  
**(as amended September 2001)**

In accordance with 37 C.F.R. § 1.121(b), Applicants submit a marked-up version of the paragraph spanning pages 23-25, in order to indicate changes Applicants have made to this paragraph.

Enhancement agents contemplated in this invention include plant growth regulators, particularly auxin-related growth regulators, which will include auxins, compounds with auxin-like activity, and auxin antagonists. Auxin-related growth regulators will typically be incorporated in the medium at concentrations of between  $10^{-10}$  M to  $10^{-3}$  M, preferably between  $10^{-8}$  to  $10^{-5}$  M. Most preferred examples of auxin-related growth regulators include 1-Naphthaleneacetic acid, 2-Naphthaleneacetic acid, 1-Naphthaleneacetamide/Naphthylacetamide, N-(1-Naphthyl)phthalamic acid, 1-Naphthoxyacetic acid, 2-Naphthoxyacetic acid, beta-Naphthoxyacetic acid, 1-Naphthoxyacetamide, 3-Chlorophenoxyacetic acid, 4-Chlorophenoxyacetic acid, [3-Iodophenoxyacetic acid] 4-Iodophenoxyacetic acid, Indoleacetamide, Indoleacetic acid, Indoylacetate, Indoleacetyl leucine, Gamma-(3-Indole)butyric acid, 4-Amino-3,5,6-trichloropicolinic acid, 4-Amino-3,5,6-trichloropicolinic acid methyl ester, 3,6-Dichloro-o-anisic acid, 3,7-Dichloro-8-quinolinecarboxylic acid, Phenylacetic acid, 2-Iodophenylacetic acid, 3-Iodophenylacetic acid, 2-Methoxyphenylacetic acid, Chlorpropham, 4-chloroindole-3-acetic acid, 5-Chloroindole-3-acetic acid, 5-Bromo-4-chloro-3-indoyl butyrate, Indoleacetyl phenylalanine, Indoleacetyl glycine, Indoleacetyl alanine, 4-chloroindole, p-chlorophenoxyisobutyric acid, 1-pyrenoxylbenzoic acid, Lysophosphatidic acid, 1-naphthyl-N-methylcarbamate, and Ethyl-5-chloro-1H-Indazole-3-ylacetate-3-Indolebutanoic acid. Other preferred examples of auxin-related growth regulators include Naphthalene-2,6-dicarboxylic acid, Naphthalene-1,4,5,8-tetracarboxylic acid dianhydride, Naphthalene-2-sulfonamide, 4-Amino-3,6-disulfo-1,8-naphthalic anhydride, 3,5-dimethylphenoxyacetic acid, 1,8-Naphthalimide, 2,4-Dichlorophenoxyacetic acid, 2,3-Dichlorophenoxyacetic acid, 2,3,5-Trichlorophenoxyacetic acid, 2-Methyl-4-chlorophenoxyacetic acid, Nitrophenoxyacetic acids, DL-alpha-(2,4-Dichlorophenoxy)propionic acid, D-alpha-(2,4-Dichlorophenoxy)propionic acid,

4-Bromophenoxyacetic acid, 4-Fluorophenoxyacetic acid, 2-Hydroxyphenoxyacetic acid, 5-Chloroindole, 6-Chloro-3-indoylacetate, 5-Fluoroindole, 5-Chloroindole-2-carboxylic acid, 3-Chloroindole-2-carboxylic acid, Indole-3-pyruvic acid, 5-Bromo-4-chloro-3-indoylbutyrate, 6-Chloro-3-indoylbutyrate, Quinoline-2-thioglycolic acid, Aminophenylacetic acids, 3-Nitrophenylacetic acid, 3-Chloro-4-hydroxybenzoic acid, Chlorflurenol, 6-Chloro-3-indoylacetate, N-(6-aminoethyl)-5-chloro-1-Naphthalenesulfonamide hydrochloride, 2-chloro-3(2,3-dichloro-phenyl) propionitrile, o-chlorophenoxyacetic acid, 6,7-dimethoxy-1,2-benzisoxazole-3-acetic acid, 3-oxo-1,2,-benzisothiazoline-2-ylacetic acid, Mastoparan, 2,3,5-Triiodobenzoic acid, 2-(3-chlorophenoxy)propanoic acid, and Mecoprop. Other examples of suitable auxin-related growth regulators include Naphthoic acid hydrazide, 2,4-Dibromophenoxyacetic acid, 3-Trifluoromethylphenoxyacetic acid, Oxindole, Indole-2-carboxylic acid, Indole-3-lactic acid, Beta-(3-Indole)propionic acid, 2-Bromophenylacetic acid, 3-Bromophenylacetic acid, 2-Chlorophenylacetic acid, 3-Chlorophenylacetic acid, 2-Methylphenylacetic acid, 3-Methylphenylacetic acid, 3-Phenylpropionic acid, 4-chloro-2-methylphenylthioacetic acid, 2-Chlorobenzoic acid, 3-Chlorobenzoic acid, 2,3-Dichlorobenzoic acid, 3,4-Dichlorobenzoic acid, 2,3,5-Trichlorobenzoic acid, 2,4,6-Trichlorobenzoic acid, 2-Benzothiazoleoxyacetic acid, 2- Chloro-3-(2,3-dichlorophenyl)propionitrile, 2,4-Diamino-s-triazine, Naphthalic anhydride, Dikegulac, chlorflurecolmethyl ester, 2-(p-chlorophenoxy)-2-methylpropionic acid, 2-chloro-9-hydroxyfluorene-9-carboxylic acid, 2,4,6-trichlorophenoxyacetic acid, 2-(p-chlorophenoxy)-2-methyl propionic acid, Ethyl 4-(chloro-o-tolyloxy)butyrate, [N-(1,3-dimethyl-1H-Pyrazol-5-yl)-2-(3,5,6-Trichloro-2-pyridinyl)oxy]acetamide, 4-Chloro-2-oxobenzothiazolin-3-yl-acetic acid, 2-(2,4-Dichlorophenoxy)propanoic acid, 2-(2,4,5-Trichlorophenoxy) propanoic acid, 4-Fluorophenylacetic acid, 3-Hydroxyphenylacetic acid, Orthonil, 3,4,5-Trimethoxycinnamic acid, 2(3,4-dichlorophenoxy)triethylamine, Indole-3-propionic acid, Sodium Ioxynil, 2-Benzothiazoleacetic acid, and (3-phenyl-1,2,4-thiadiazol-5-yl)thioacetic acid.

**APPENDIX B**  
**VERSION OF CLAIMS WITH MARKINGS**  
**U.S. Application No. 08/479,809**  
**(as amended September 2001)**

In accordance with 37 C.F.R. § 1.121(c), Applicants submit a marked-up version of the claims, in order to indicate changes Applicants have made.

1. ([twice]thrice amended) A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein at least one of the one or more nutrient media comprises one or more enhancement agents selected from the group consisting of (a) jasmonate-related compounds [an]or alkyl esters thereof, (b) antiethylene agents, and (c) inhibitors of phenylpropanoid metabolism.

2. The method of claim 1, wherein the one or more nutrient media contain an antiethylene agent which is a silver-containing compound, or a silver complex, or a silver ion.

3. (twice amended) The method of claim 1, wherein a jasmonate-related compound or an alkyl ester thereof is added to the one or more nutrient media.

6. (amended) The method of claim 3, wherein the jasmonate-related compound is in a concentration from  $10^{-5}$  to  $2 \times 10^{-4}$  M.

7. (amended) The method of claim 3, wherein the jasmonate-related compound is at least one compound selected from the group consisting of jasmonic acid, dihydrojasmonic acid.

8. The method of claim 3, wherein the jasmonate-related compound is at least one compound selected from the group consisting of jasmonic acid and alkyl esters of jasmonic acid.

9. (twice amended) The method of claim 8, wherein said alkyl ester of jasmonic acid comprises an alkyl group esterified to jasmonic acid wherein said alkyl group has from one to four carbon atoms.

10. The method of claim 8, wherein the alkyl group esterified to jasmonic acid has one carbon atom.

11. The method of claim 3, wherein the cells are cultured in the presence of heavy metal ions, heavy metal complexes, or heavy metal-containing compounds.

12. (amended) The method of claim 11, wherein the heavy metal ions are cobalt ions, the heavy metal complexes are cobalt complexes, and the heavy metal-containing compounds are cobalt-containing compounds.

13. (amended) The method of claim 3, wherein the cells are cultured in the presence of an antiethylene agent.

14. The method of claim 13, wherein the antiethylene agent is an ethylene-biosynthesis antagonist.

15. The method of claim 14, wherein the ethylene-biosynthesis antagonist is a compound which inhibits ACC synthase, ACC oxidase, or ethylene oxidase.

16. The method of claim 14, wherein the ethylene-biosynthesis antagonist is acetylsalicylic acid or aminoxyacetic acid.

17. The method of claim 13, wherein the antiethylene agent is an ethylene-action antagonist.

18. The method of claim 17, wherein the ethylene-action antagonist is a silver-containing compound, a silver complex or silver ion.

19. (amended) The method of claim 18, wherein the silver-containing compound is at least one compound selected from the group consisting of silver thiosulfate, silver chloride, and silver oxide.

20. (amended) The method of claim 18, wherein the silver-containing compound is at least one compound selected from the group consisting of silver phosphate, silver benzoate, toluenesulfonic acid silver salt, silver acetate, silver nitrate, and silver sulfate.

21. (amended) The method of claim 18, wherein the silver-containing compound is at least one compound selected from the group consisting of silver pentafluoropropionate, silver cyanate, lactic acid silver salt, silver hexafluorophosphate, citric acid trisilver salt, and silver nitrite.

24. (twice amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, [and]or silver-containing compounds is 10 $\mu$ M – 100 $\mu$ M

25. (twice amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, [and]or silver-containing compounds is 50  $\mu$ M.

26. (twice amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, [and]or silver-containing compounds is 10 $\mu$ M.

27. (amended) The method of claim 18, wherein [the molar ratio of ]silver [to jasmonic acid]and jasmonate are present in the one or more nutrient media [is]in molar ratio of silver: jasmonate of less than 9.5.

28. The method of claim 1, wherein the one or more nutrient media contain an inhibitor of phenylpropanoid metabolism.

29. (amended) The method of claim 28, wherein the inhibitor of phenylpropanoid metabolism is selected from the group consisting of 3,4-methylenedioxynitrocinnamic acid 3,4-methylenedioxycinnamic acid, 3,4-methylenedioxy-phenylpropionic acid, 3,4-methylenedioxypyrenylacetic acid, 3,4-methylenedioxybenzoic acid, 3,4-trans-dimethoxycinnamic acid, 4-hydroxycinnamic acid, phenylpropionic acid, fluorophenylalanine, 1-aminobenzotriazole, 2-hydroxy-4,6-dimethoxybenzoic acid, [SKF]2-[525A](diethylamino)ethyl ester of  $\alpha$ -phenyl- $\alpha$ -propylbenzeneacetic acid, ammonium oxalate, vinylimidazole, diethyldithiocarbamic acid, and sinapic acid.

30. The method of claim 1, wherein the one or more nutrient media contain at least one enhancement agent selected from each of at least two of the following classes of enhancement agents: (a) jasmonic acid or an alkyl ester thereof, (b) antiethylene agents, and (c) inhibitors of phenylpropanoid metabolism.

31. The method of claim 30, wherein the jasmonic acid alkyl ester is methyl jasmonate.

32. [32.] (amended) The method of claim 1 or claim 30, wherein the one or more nutrient media further comprise an auxin-related growth regulator[.] selected from the group consisting of 1-Naphthaleneacetic acid, 2-Naphthaleneacetic acid, 1-Naphthaleneacetamide/ Naphthylacetamide, N-(1-Naphthyl)phthalamic acid, 1-Naphthoxyacetic acid, 2-Naphthoxyacetic acid, beta-Naphthoxyacetic acid, 1-

Naphthoxyacetamide, 3-Chlorophenoxyacetic acid, 4-Chlorophenoxyacetic acid, 4-Iodophenoxyacetic acid, Indoleacetamide, Indoleacetic acid, Indoylacetate, Indoleacetyl leucine, Gamma-(3-Indole)butyric acid, 4-Amino-3,5,6-trichloropicolinic acid, 4-Amino-3,5,6-trichloropicolinic acid methyl ester, 3,6-Dichloro-o-anisic acid, 3,7-Dichloro-8-quinolinecarboxylic acid, Phenylacetic acid, 2-Iodophenylacetic acid, 3-Iodophenylacetic acid, 2-Methoxyphenylacetic acid, Chlorpropham, 4-chloroindole-3-acetic acid, 5-Chloroindole-3-acetic acid, 5-Bromo-4-chloro-3-indoyl butyrate, Indoleacetyl phenylalanine, Indoleacetyl glycine, Indoleacetyl alanine, 4-chloroindole, p-chlorophenoxyisobutyric acid, 1-pyrenoxylbenzoic acid, Lysophosphatidic acid, 1-naphthyl-N-methylcarbamate, Ethyl-5-chloro-1H-Indazole-3-ylacetate-3-Indolebutanoic acid, Naphthalene-2,6-dicarboxylic acid, Naphthalene-1,4,5,8-tetracarboxylic acid dianhydride, Naphthalene-2-sulfonamide, 4-Amino-3,6-disulfo-1,8-naphthalic anhydride, 3,5-dimethylphenoxyacetic acid, 1,8-Naphthalimide, 2,4-Dichlorophenoxyacetic acid, 2,3-Dichlorophenoxyacetic acid, 2,3,5-Trichlorophenoxyacetic acid, 2-Methyl-4-chlorophenoxyacetic acid, Nitrophenoxyacetic acids, DL-alpha-(2,4-Dichlorophenoxy)propionic acid, D-alpha-(2,4-Dichlorophenoxy)propionic acid, 4-Bromophenoxyacetic acid, 4-Fluorophenoxyacetic acid, 2-Hydroxyphenoxyacetic acid, 5-Chloroindole, 6-Chloro-3-indoylacetate, 5-Fluoroindole, 5-Chloroindole-2-carboxylic acid, 3-Chloroindole-2-carboxylic acid, Indole-3-pyruvic acid, 5-Bromo-4-chloro-3-indoylbutyrate, 6-Chloro-3-indoylbutyrate, Quinoline-2-thioglycolic acid, Aminophenylacetic acids, 3-Nitrophenylacetic acid, 3-Chloro-4-hydroxybenzoic acid, Chlorflurenol, 6-Chloro-3-indoyl acetate, N-(6-aminohexyl)-5-chloro-1-Naphthalenesulfonamide hydrochloride, 2-chloro-3(2,3-dichloro-phenyl) propionitrile, o-chlorophenoxyacetic acid, 6,7-dimethoxy-1,2-benzisoxazole-3-acetic acid, 3-oxo-1,2-benzisothiazoline-2-ylacetic acid, Mastoparan, 2,3,5-Triidobenzoic acid, 2-(3-chlorophenoxy)propanoic acid, Mecoprop, Naphthoic acid hydrazide, 2,4-Dibromophenoxyacetic acid, 3-Trifluoromethylphenoxyacetic acid, Oxindole, Indole-2-carboxylic acid, Indole-3-lactic acid, Beta-(3-Indole)propionic acid, 2-Bromophenylacetic acid, 3-Bromophenylacetic acid, 2-Chlorophenylacetic acid, 3-Chlorophenylacetic acid, 2-Methylphenylacetic acid, 3-Methylphenylacetic acid, 3-Trifluoromethylphenylacetic acid, 3-Methylthiophenylacetic acid, Phenylpropionic acid,

4-chloro-2-methylphenylthioacetic acid, 2-Chlorobenzoic acid, 3-Chlorobenzoic acid, 2,3-Dichlorobenzoic acid, 3,4-Dichlorobenzoic acid, 2,3,5-Trichlorobenzoic acid, 2,4,6-Trichlorobenzoic acid, 2-Benzothiazoleoxyacetic acid, 2-Chloro-3-(2,3-dichlorophenyl)propionitrile, 2,4-Diamino-s-triazine, Naphthalic anhydride, Dikegulac, chlorflurecolmethyl ester, 2-(p-chlorophenoxy)-2-methylpropionic acid, 2-chloro-9-hydroxyfluorene-9-carboxylic acid, 2,4,6-trichlorophenoxyacetic acid, 2-(p-chlorophenoxy)-2-methyl propionic acid, Ethyl 4-(chloro-o-tolyloxy)butyrate, [N-(1,3-dimethyl-1H-Pyrazol-5-yl)-2-(3,5,6-Trichloro-2-pyridinyl)oxy]acetamide, 4-Chloro-2-oxobenzothiazolin-3-yl-acetic acid, 2-(2,4-Dichlorophenoxy)propanoic acid, 2-(2,4,5-Trichlorophenoxy) propanoic acid, 4-Fluorophenylacetic acid, 3-Hydroxyphenylacetic acid, Orthonil, 3,4,5-Trimethoxycinnamic acid, 2(3,4-dichlorophenoxy)triethylamine, Indole-3-propionic acid, Sodium Ioxynil, 2-Benzothiazoleacetic acid, and (3-phenyl-1,2,4-thiadiazol-5-yl)thioacetic acid.

33. The method of claim 30, wherein the antiethylene agent is a silver-containing compound, a silver complex or silver ion.

34. (amended) The method of claim 30, wherein the inhibitor of phenylpropanoid metabolism is selected from the group consisting of 3,4,-methylenedioxynitrocinnamic acid, 3,4,-methylenedioxycinnamic acid, 3,4,-methylenedioxy-phenylpropionic acid, 3,4,-methylenedioxyphenylacetic acid, 3,4-methylenedioxybenzoic acid, 3,4,-trans-dimethoxycinnamic acid, 4-hydroxycinnamic acid, phenylpropionic acid, fluorophenylalanine, 1-aminobenzotriazole, 2-hydroxy-4,6-dimethoxybenzoic acid, [SKF]2-[525A](diethylamino)ethyl ester of  $\alpha$ -phenyl- $\alpha$ -propylbenzeneacetic acid, ammonium oxalate, vinylimidazole, diethyldithiocarbamic acid, and sinapic acid.

35. (amended) The method of claim 1, claim 3, or claim 30, wherein the one or more nutrient media further comprises a polyamine.

36. The method of claim 35, wherein the polyamine is selected from the group consisting of spermine, spermidine, putrescine, cadaverine, and diaminopropane.

37. The method of claim 1 or claim 30, wherein the one or more nutrient media further comprise a taxane precursor.

38. The method of claim 32, wherein the auxin-related growth regulator is picloram, indoleacetic acid, 1-naphthaleneacetic acid, indolebutyric acid, 2,4-dichlorophenoxyacetic acid, 3,7-dichloro-8-quinolinecarboxylic acid, or 3,6-dichloro-o-anisic acid.

39. (amended) The method of claim 1, wherein the amount of said one or more taxanes recovered is at least 3-fold greater than the amount obtained from cells of *Taxus* species cultured without addition of any enhancement agents selected from the group consisting of (a) jasmonate-related compounds or alkyl esters thereof, (b) anti-ethylene agents, and (c) inhibitors of [phylpropanoid]phenylpropanoid metabolism.

40. (amended) The method of claim 1, wherein the amount of said one or more taxanes recovered is at least 5-fold greater than the amount obtained from cells of *Taxus* species cultured without addition of any enhancement agents selected from the group consisting of (a); [asmonate]jasmonate-related compounds or alkyl esters thereof, (b) anti-ethylene agents, and (c) inhibitors of [phylpropanoid]phenylpropanoid metabolism.

41. (twice amended) The method of claim 1, wherein said one or more taxanes recovered is at least one compound selected from the group consisting of taxol, 7-epitaxol, 10-deacetyl-7-epitaxol, cephalomannine, 10-deacetyltaxol, 7-xylosyl-10-deacetyltaxol, baccatin III, and 10-deacetyl baccatin III.

42. (twice amended) The method of claim 1, wherein the cells are cultured in a first medium having a first composition, then the medium composition is changed to a second medium having a second composition which induces taxane production.

43. (twice amended) The method of claim 42, wherein the concentration of nitrate is lower in the second medium than in the first medium, and the concentration of a saccharide is higher in the second medium than in the first medium.

44. (amended) The method of claim 43, wherein the first medium contains nitrate at a concentration which is 2 to 10 times the nitrate concentration in the second medium.

45. (twice amended) The method of claim 42, wherein the second medium contains a saccharide at a concentration which is 2 to 5 times the saccharide concentration in the first medium.

46. ([thrice ]amended four times) The method of claim 1, wherein the cells are cultured in media containing a saccharide in a concentration of 1 – 150 g/L, nitrate ion in a concentration of 0.3 – 70 mM or a combination thereof.

47. (twice amended) The method of claim 43, wherein the first medium contains a saccharide in the concentration of 1 – 30 g/L, and nitrate ion in the concentration of 2.5 – 70 mM; and the second medium containsa saccharide in the concentration of 4 – 150 g/L, and nitrate ion in the concentration of 0.3 – 18 mM.

48. (twice amended) The method of claim 43, wherein the first medium contains a saccharide in the concentration of 5 – 15 g/L, and nitrate ion in the concentration of 20 – 30 mM; and the second medium containsa saccharide in the concentration of 35 – 55 g/L, and nitrate ion in the concentration of 2 – 7 mM.

49. (twice amended) The method of claim 42, wherein the medium which induces taxane production is replenished during cultivation by periodically replenishing nutrient medium components and removing spent medium.

50. (amended) The method of claim 1 or claim 30, wherein said [step of cultivating further comprises exchanging nutrient]the medium [at least once]which induces taxane production is replenished during [the ]cultivation [step]by periodically replenishing nutrient medium components and removing spent medium.

51. The method of claim 1 or claim 30, wherein nutrient medium is the same for cell culture growth and for taxane production.

52. The method of claim 1 or claim 30, wherein cells of said *Taxus* species are cultivated by a continuous or semi-continuous process.

53. (amended) The method of claim 1, claim 3, or claim 30, wherein cells of said *Taxus* species are cultivated by a fed-batch process.

54. (twice amended) The method of claim 53, wherein the culture medium is replenished during cultivation by periodically replenishing nutrient medium components and removing spent medium.

55. (amended) The method of claim 1 or claim 30, further comprising the periodic removal of said at least one or more taxanes from the nutrient media.

56. The method of claim 1 or claim 30, wherein the *Taxus* species is selected from the group consisting of *T. canadensis*, *T. chinensis*, *T. cuspidata*, *T. baccata*, *T. globosa*, *T. floridana*, *T. wallichiana*, and *T. media*.

57. The method of claim 3 or claim 30, wherein the *Taxus* species is *Taxus brevifolia*.

58. The method of claim 1, wherein the cells are cultured in the presence of 0.03% to 15% v/v of carbon dioxide in the gas phase in equilibrium with the culture medium.

59. (amended) The method of claim 1 or claim 3, wherein the cells are cultured in the presence of 0.3% to 8% v/v of carbon dioxide in the gas phase in equilibrium with the culture medium.

60. The method of claim 1, wherein the cells are cultured in the presence of controlled oxygen concentration between 1% to 200% of air saturation.

61. The method of claim 1, wherein the cells are cultured in the presence of controlled oxygen concentration between 10% to 100% of air saturation.

62. (amended) The method of claim 1 or claim 3, wherein the cells are cultured in the presence of controlled oxygen concentration between 25% to 95% of air saturation.

63. The method of claim 42, wherein the second medium comprises a ] jasmonate-related compound or an alkyl ester thereof.

64. The method of claim 1 or claim 30, wherein a jasmonate-related compound or an alkyl ester thereof is added continuously to the cell culture.

65. The method of claim 1 or claim 30, wherein the one or more nutrient media contain glutamine.

66. (amended) The method of claim 3, wherein the cells are cultured in media containing saccharide in a concentration of 1 – 150 g/L, nitrate ion in a concentration of 0.3 – 70 mM or a combination thereof.

67. The method of claim 1, wherein the one or more nutrient media contain an antiethylene agent.

68. (amended) A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more

nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein at least one of the one or more nutrient media comprises a compound selected from the group consisting of [(a) amino acids and (b) ]polyamines.

69. (twice amended) The method of claim 68, wherein said [amino acids, said ]polyamines[, or a combination thereof] are added to at least one of the one or more nutrient media.

70. A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein cells of said *Taxus* species are cultured in the presence of controlled oxygen concentration between 10% to 100% of air saturation.

71. (amended) The method of claim 2, wherein the concentration of silver ions, silver complexes, [and]or silver-containing compounds is 0.01  $\mu\text{M}$  – 10  $\mu\text{M}$ .

72. (amended) A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein  $\beta$ -phenylalanine is added to the one or more nutrient media in an amount sufficient to enhance taxane production.